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# Sunscreen effectivity and physical characterization of avocado oil in nanoemulsion using isopropyl myristate variations

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## ABSTRACT

Unsaturated fatty acids in avocado oil can help reduce erythema brought on by prolonged UV-B exposure. The effectivity of sunscreen absorption into the skin will be enhanced by the use of isopropyl myristate (IPM) in nanoemulsion. The purpose of this study was to determine the physical characteristics and sunscreen effectiveness of avocado oil nanoemulsion (AVN) modified with IPM. 1% (FI), 3% (FII), and 5% (FIII) IPM variation were used to make AVN with 5% oil. The AVN were tested for physical characteristics such as organoleptic, pH, viscosity, rheology, particle size and polydispersity index (PI). The products were also tested for sunscreen effectivity by in vitro and Minimum Erythemal Dose (MED) method. The data obtained were analyzed statistically. The results showed that the AVN was pale yellow and clear with transmittance percentage were 96%. The rheogram showed that the products were newtonian. The pH values range were from 6.62 to 6.66; viscosity 1.65-1.84 dPa.s; particle size < 17 nm, zeta potential was in range of -30,54±1,72 to -37,85±3,11 and PI < 0.5 for all formula. In vitro SPF values were 16.43 ± 4.50 (FI), 16.27 ± 4.20 (FII) and 17.88 ± 3.20 (FIII) ($p > 0.05$), and categorized as ultra protection. MED value were 12.28 ± 1.34 (FI); 12.51 ± 1.68 (FII); and 13.22 ± 1.84 (FIII) ($p < 0.05$) and categorized as maximum protection. Isopropyl myristate increased the sunscreen product's MED value without changing its physical characteristics.

**Keywords**: avocado oil, enhancer, erythema, nanoemulsion

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## INTRODUCTION

Chemical sunscreen absorbs sun rays and converts it into heat energy. This sunscreen can work after being absorbed into the skin, so it has the potential to irritate (Minerva, 2019). Sunscreen functions by either scattering or absorbing solar energy to prevent it from striking the skin directly (Riascos, 2012). The effectivity of sunscreen is expressed as SPF value of more than 10, thus describing its ability to prevent erythema due to sun exposure (Araújo et al., 2016). FDA has prohibited sunscreen that contains Para Amino Benzoic Acid (PABA), avobenzone and its derivate due to its side effect (Pirotta, 2020). PABA has the potential to cause many hormone disorders and breast cancer through skin absorption (Barel et al., 2009). Active compound such as Z-3, octyl-methoxycinnamate will increase luteinizing hormone. Due to this side effect, it is necessary to develop natural sunscreen.

One natural component that may be utilized to prepare sunscreen and absorb UV-B radiation is avocado oil (Flores et al., 2019). Avocado oil has bioactive components that benefit the skin such as palmitic acid and linoleic acid, which can increase skin moisture and prevent skin erythema (Li et al., 2019). Components of avocado oil are also used to heal inflammation and skin erythema through skin barrier repair mechanisms (De Oliveira et al., 2013). Previous study had been shown that avocado oil has sunscreen activity with SPF value of 6 to 16 (Fares et al., 2023).

Nanoemulsion system is one of a promising delivery system for cosmetics. For topical usage, this system has good stability and skin penetration capabilities, particularly for active ingredients derived from essential or plant oils (Mohite et al., 2019). Nanoemulsion system can reduce the globule size and increase the efficacy of oil in cosmetic preparations (Hashim et al., 2019). Preparations that are applied topically, such as sunscreen, must be absorbed quickly by the skin to provide a good therapeutic effect (Argenta et al., 2014). Enhancers like isopropyl myristate (IPM) can be added to improve the absorption of active ingredients (Eichner et al., 2017).

Due to the low surface tension and viscosity, isopropyl myristate (IPM) can increase the physical characteristics of nanoemulsion. IPM fits the properties of nanoemulsions, which have a globule size of less than 1000 nm, and is useful in the production of nanoemulsions because of its low molecular weight (Souto et al., 2022). To stabilize the nanoemulsion during storage, intergranular agglomeration can be avoided by adding IPM to the nanoemulsion formula. When IPM and Tween 80 surfactant are used together, the penetration of the active ingredients can be increased, improving the efficacy of the product (Sondari & Tursiloadi, 2018). Based on the background above, it is necessary to characterize and study the effectivity of avocado oil in nanoemulsion using IPM as an enhancer.

## MATERIALS AND METHOD

### Materials and tools

A magnetic stirrer (Scilogex®), a pH meter (Electro Lab®), a vortex, a nonirritant bandage (Hypafic®), a cone and plate viscometer (Rheosys Merlin VR II®), a particle size analyzer (SZ-100®), a pH spectrophotometer (Shimadzu®), and sterile gauze (Onemed®) were the instruments used in this study.

The primary component of this study was cosmetic-grade avocado oil, which was acquired with an analytical certificate from PT. Daarjeling, Bandung. The carrier materials utilized were methanol with analytical grade acquired from CV. Multi Kimia Raya, Semarang, tween 80, PEG 400, isopropyl myristate, and benzyl alcohol with cosmetic grade. The Parasol SPF 25++ Spray Sunscreen is the comparison utilized.

The test animals used in the research were 3 rabbits. Inclusion criteria were male, 3 months old, with weight at 1,5-2 kg, in good health condition, with strain of New Zealand White. This test had obtained ethical clearance from the Faculty of Medicine and Health Sciences, Muhammadyah University of Yogyakarta with number: 014/EC-KEPK FKIK UMY/III/2023.

## Methods

### Avocado oil nanoemulsion formula with variations of isopropyl myristate

Table 1 displays the formula for the nanoemulsion of avocado oil. The temperature of the purified water was raised to 30°C. Benzyl alcohol was dissolved in water and agitated until it was homogenous using a magnetic stirrer running at 700 rpm. In order to create a homogenous mixture, Tween 80 and PEG 400 were added to a solution of benzyl alcohol and filtered water during the first mixing stage. Avocado oil and isopropyl myristate were mixed in the second stage until a clear and transparent nanoemulsion was formed. The second stage of mixing was carried out at a speed of 1000 rpm for 30 minutes.

**Table 1. Avocado oil nanoemulsion formula** (Shabrina & Khansa, 2022)

| Components | Concentration (%) | | |
|---|---|---|---|
| | **F1** | **F2** | **F3** |
| Avocado oil | 5 | 5 | 5 |
| Isopropyl Myristate | 1 | 3 | 5 |
| Tween 80 | 40 | 40 | 40 |
| PEG 400 | 30 | 30 | 30 |
| Benzyl alcohol | 1 | 1 | 1 |
| Purified Water | | up to 100 | |

### Evaluation of physical properties of avocado oil nanoemulsion

The color, odor, and phase separation of the avocado oil nanoemulsion were visually observed in order to conduct an organoleptic examination. The pH of the nanoemulsion was measured using 10 milliliters of sample and a pH meter that had been calibrated in a buffer solution with pH values of 4 and 7. 5 mL of the sample was put into a cone and plate type viscometer and rotated six times at a speed of 12 rpm for 30 seconds each to measure the viscosity and rheology. Three milliliters of the sample were put in a cuvette to test the sample's clarity, and a spectrophotometer was used to determine the transmittance %. Using a Particle Size Analyzer (PSA) and zeta sizer with 5 mL samples, tests for particle size, polydispersity index (PI), and zeta potential were conducted. Every test was conducted three times (Shabrina et al., 2022).

### Effectivity test of avocado oil nanoemulsion

The first step in determining SPF is to compute the Correction Factor (CF) value by comparing it to Parasol SPF 25++. Each of the following: FI, FII, FIII, and Parasol SPF 25++ were measured out to a maximum volume of 0.5 mL, placed in a 10 mL flask, methanol PA was added to the mark, and the mixture was homogenized with a vortex. A UV spectrophotometer was used to measure the absorbance between 290 and 320 nm, and the absorbance values were noted at every 5 nm interval. The CF value was computed by using the Mansur formula to the received results.

The Minimum Erythema Dose (MED) was used to determine the effectiveness of sunscreen. The test rabbits' hair was shaved off with a shaver 24 hours before to treatment. Five treatment locations were marked on the backs of the shaved animals: FI, FII, FIII, comparison (Parasol SPF 25++), and no treatment. Every test point was identified using a 4x4 cm marker. 311 nm UV light was given to the test animals. We counted the quantity of erythema (red spots) that developed in every test animal group. Minimum Erythema Dose (MED) is the amount of UV light exposure time that elapsed before the erythema appeared. The efficiency of sunscreen was calculated by comparing the MED of exposed skin with skin shielded by preparation and Parasol SPF 25++ (Costa et al., 2015; Heckman et al., 2013).

**Data Analysis**

One way ANOVA was used to statistically assess the data on pH, viscosity, transmittance percentage, particle size, polydispersity index, and zeta potential and SPF value for each formula. The sunscreen effectivity was calculated by independent t-test analysis of in vitro SPF and MED value data.

**RESULT AND DISCUSSION**

Figure 1 depicts the physical characteristics of the avocado oil nanoemulsion. Table 2 displays the physical properties of the avocado oil nanoemulsion. The findings demonstrated that the pH range of all avocado oil nanoemulsion formulas was 4.5–8.0, which is appropriate for topical applications (Badan Standarisasi Nasional, 1996). The pH of avocado oil before formulation was 6.70 ± 1.50. Additional ingredients such as surfactants, cosurfactants and enhancers had a pH range of 6.0-7.5. The system experienced an increase in pH after avocado oil was incorporated in nanoemulsion yet did not differ significantly. The preparation will cause a skin irritation if the pH is below 4,2 (BPOM, 2014). The pH results of the preparation met the SNI standards for sunscreen preparations. The results showed that increasing the IPM concentration did not affect the pH of the preparation ($p > 0.05$). The results of the viscosity values can be seen in Table 2.

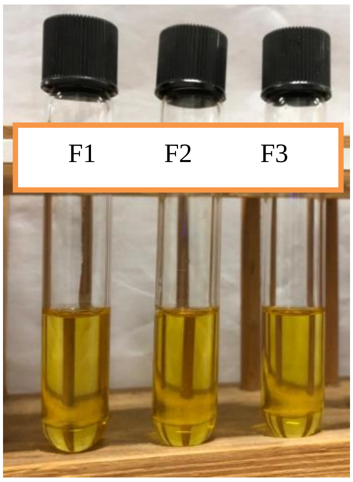


**Figure 1. The nanoemulsion of avocado oil**

**Table 2. Avocado oil nanoemulsion's physical characteristics with IPM variation**

| Formula | Physical characteristics | | | | | |
|---|---|---|---|---|---|---|
| | pH | Viscosity (d.Pas) | Transmittance Percentage (%) | Particle Size (nm) | Polydispersity Index | Zeta Potential (Mv) |
| FI | 6.66±0.03 | 1.75 ± 0.87 | 96.50 ± 1.51 | 15.50 ± 2.13 | 0.476 ± 0.215 | -32.33±2.30 |
| FII | 6.65±0.04 | 1.84 ± 0.83 | 96.70 ± 1.53 | 14.75 ± 1.41 | 0.331 ± 0.227 | -30.54±1.72 |
| FIII | 6.62±0.03 | 1.65 ± 0.84 | 96.90 ± 1.28 | 13.25 ± 1.35 | 0.213 ± 0.234 | -37.85±3.11 |

Data displayed were 3 replications with standard deviation

A low viscosity will improve the product's spreadability and user compliance when applied topically. The preparation's viscosity will rise when IPM and Tween 80 are used together as a surfactant (Goyani et al., 2018). This condition can improve the stability of the product due to the inability of globules entrapment and aggregation (Thomas et al., 2014). Compared to other mineral oils, IPM has lower viscosity and interfacial tension, which makes it easier to create small globule sizes for creating nanoemulsions (Muthi et al., 2016). IPM has the ability to attach to hydrophilic ester groups in the lipid bilayer and integrate with it, making the stratum corneum bilayer membrane's structure more brittle.

IPM belongs to the fatty acid ester group which meets safety requirements and is widely used as an enhancer (Abdullah et al., 2022). Figure 2 showed the outcomes of the rheology analysis of the avocado oil nanoemulsion. Every formula for avocado oil nanoemulsion was Newtonian. According to Marques et al. (2018), a fluid with this rheology has a velocity gradient that is perpendicular to the shear stress and a linearly proportional shear stress. These findings demonstrated that the preparation resembles a solution or liquid that flows readily since the droplets generated were smaller than emulsion (Hasrawati et al., 2016).

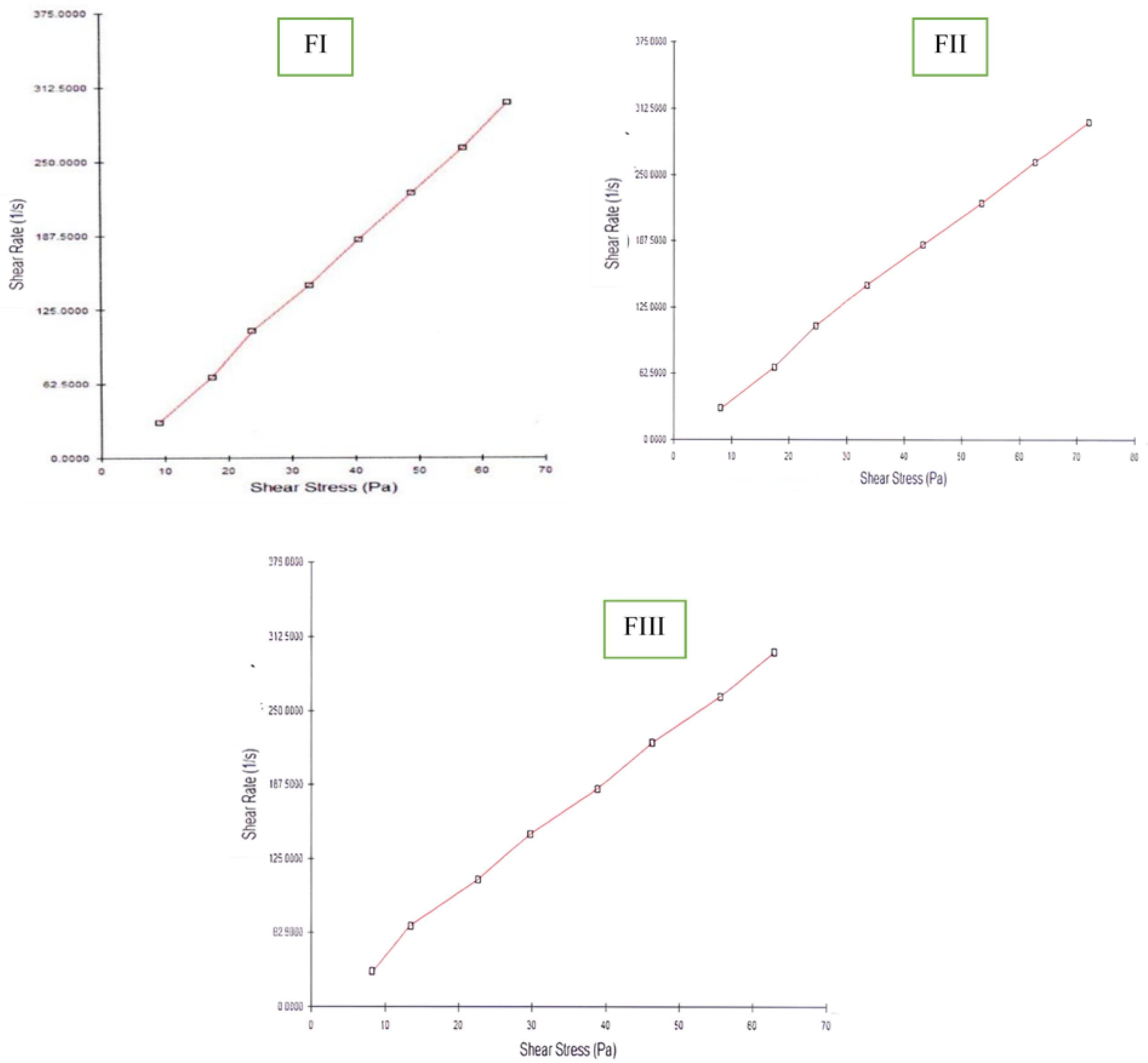


**Figure 2. The newtonian rheogram result of avocado oil nanoemulsion with IPM variations**

In mixed micelle nanoemulsion formulations, medium chain fatty acids, including IPM, have been employed as permeability enhancers and to promote good absorption of active ingredients (Zhao et al., 2016). Isopropyl myristate when combined with Tween as surfactant will increase the viscosity of the preparation (Sun et al., 2012; Zhao et al., 2016).

Nanoemulsion had a clear and transparent visual appearance with a high transmittance percentage. Nanoemulsions system with smaller dispersed droplet sizes can reduce globule agglomerations to produce a transparent product. This parameter was determined as transmittance value (%T) nanoemulsion preparations so that transparency can be formed and the percent transmittance value (%T) (Lv et al., 2018). For nanoemulsion, 90–100% percent transmittance is the optimal range (Gurpreet & Singh, 2018). Table 2 showed that the transmittance percentage satisfies the specifications needed for the perfect nanoemulsion. The results of the statistical test indicate that each formula's transmittance % was similar. The preparation of the avocado oil nanoemulsion remained transparent and clear despite variations in the IPM content.

Particle sizes in a suitable nanoemulsion range from 10 to 100 nm (Chen et al., 2017). All avocado oil nanoemulsion formula had particles smaller than 100 nm, according to Table 2's data. This occurs as a result of IPM and surfactant-cosurfactant interaction. In order to facilitate the creation of small particle sizes, Tween 80 and PEG 400 combined with IPM work by the surfactant adsorping the oil and water contact (Cho, 2016; Dalibera et al., 2021). The smaller the globule size will give a slow aggregation of the particles so that creaming in the nanoemulsion can be prevented (Mariadi et al., 2019). The small particle size can extend the shelf life of nanoemulsion preparations, besides that the preparations are not easily damaged and are more easily absorbed by the body (Dwipayana et al., 2022). The globule size results showed that there was a decrease in each formula but it was not significant. IPM is a triglyceride oil that is capable of producing low globule sizes in nanoemulsion systems (De Azevedo Ribeiro et al., 2015).

The PI value < 1 indicates that the nanoemulsion is monodisperse (Eid et al., 2013). The PI value has a correlation with particle size and zeta potential (Gaber et al., 2023). The results of this PI value are in line with previous research that a low PI value indicates a monodispersion system (Caya et al., 2020). Based on Table 2, it is known that variations in IPM concentration did not affect the PI value.

Based on the Table 2, the zeta potential showed that all formula had negative potential. The good zeta potential was close to 30 mv or -30 mv (Shakeel et al., 2021). The statistical analysis showed that there were no significant different of the zeta potential between each formula. The zeta potential of avocado oil nanoemulsion was still fulfill the requirement of nanoemulsion characteristics (Rachman et al., 2023). IPM at 3-5% in formula will show negative zeta potential from -22.5 until -34.6 mV (Abdullah et al., 2022). The zeta potential result that close to zero (0) will intend the short term stability of nanoemulsion and increase the particle aggregation during the storage (Maha & Sinaga, 2018).

**The results of the effectiveness of avocado oil nanoemulsion sunscreen using in vitro and MED methods**

Their chemical structure, which consists of an aromatic molecule coupled with a carbonyl group, determines the sunscreen's efficacy. This structure facilitates the absorption of high-energy UV radiation, leading to an excited state. The lower energy connected to longer wavelengths is released as the molecule returns to its ground state (Aguilera et al., 2023). A sunscreen's specific wavelength range of absorption varies. In order for topical sunscreen application to effectively prevent sunburn, nourish the skin, and have a photoprotective impact, it must be absorbed into the skin layers (Reza et al., 2023). The use of nanoemulsion systems is one technique for improving sunscreen penetration into the skin. When compared to sunscreen in cream or emulgel, sunscreen in nanoemulsion system has a faster transdermal absorption rate (Chavda et al., 2023).

The results of sunscreen effectivity can be seen in Table 3. A sunscreen product with a known SPF value was used to calculate the correction factor. In order to provide accurate findings, this correction factor served as a tolerance limit for the spectrophotometer and solvent usage. The Parasol cooling mist sun SPF 25+ PA++® product yielded a correction factor result of 6.68.

All formulations had significant differences, according to the findings of the independent t-test conducted by comparing the SPF values obtained from MED and in vitro experiments. The lack of suitable techniques for evaluating sunscreen products is one factor that may affect the measurement of SPF values in vitro (Zarkogianni & Nikolaidis, 2016). The determination of the SPF value of sunscreen in vitro and MED can differ depending on the combination and concentration of the sunscreen, the type of emulsion, the solvent used to dissolve the sunscreen, and the interaction of other additional components like emulsifiers in a formulation (Heckman et al., 2013; Kausar et al., 2017).

**Table 3. Results of SPF values using the MED and in vitro methods**

| Formula | MED (minutes) | SPF based on MED | Category based on MED Data | SPF in vitro | Kategori SPF in vitro | P Value of In vitro SPF and MED |
|---|---|---|---|---|---|---|
| Unprotected Skin | 13.5 ± 7.41 | - | - | - | - | - |
| FI | 221.5 ± 6.24[c.d] | 16.43 ± 4.50 [c.d] | Ulta Protection | 12.28 ± 1.34 | Maximum Protection | 0.032 |
| FII | 228.4 ± 5.31 [c.d] | 16.27 ± 4.20 [c.d] | | 12.51 ± 1.68 | | |
| FIII | 248.2 ± 3.45[a.b.d] | 17.88 ± 3.20 [a.b.d] | | 13.22 ± 1.84 | | |
| Parasol® | 326.2 ± 4.60[a.b.c] | 24.51 ± 4.60 [a.b.c] | | 6.68 ± 3.41[a.b.c] | | |

Notes
n = 3 ± standard deviation
a: Significantly different with F1
b: Significantly different with F2
c: Significantly different with F3
d: Significantly different with Parasol®

According to the findings of the one-way ANOVA test on SPF values based on MED, FI and FII differed significantly from FIII in terms of SPF values. This demonstrates how changes in IPM concentration can lengthen the MED period and result in a higher SPF value. When IPM is present, product absorption into the skin can be enhanced. Sunscreen made of natural substances can work well as long as the preparation is absorbed by the skin (Barradas & de Holanda e Silva, 2021). Elevated concentrations of isopropryl myristate have the ability to break down the inflexible lipid structure and lessen the tension in the stratum corneum, which increases penetration and makes it easier for the active ingredient to enter the skin layers (Jiang et al., 2017). In addition, isopropyl myristate serves as a co-surfactant in the nanoemulsion formulation, giving the final nanoemulsion formula good stability (Dalibera et al., 2021).

The active ingredient components of the avocado oil nanoemulsion can be absorbed by using IPM in conjunction with surfactants and cosurfactants, such as tween 80 and PEG 400, because the nanoemulsion's smaller droplet size can improve the active ingredient's ability to permeate the membrane (Iliopoulos et al., 2022; Pakki et al., 2019). Tween and PEG 400 play an important role in the ability of nanoemulsions to release active ingredients by influencing the surface layer of the nanoemulsion (Akhtar et al., 2011; Nastiti et al., 2017).

## CONCLUSION

Avocado oil nanoemulsion has a clear appearance and meets the criteria for a nanoemulsion delivery system. Isopropyl myristate does not affect the physical characteristics of the preparation and at a concentration of 5% shows the highest sunscreen effectiveness.

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